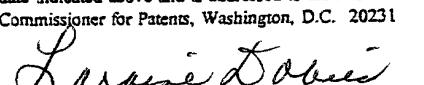


U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE (REV. NO. 04)		ATTORNEY'S DOCKET NUMBER <b>990667/RSB</b>
<b>TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371</b>		U.S. APPLICATION NO. (If known, see 37 CFR 1.5) <b>09/403940</b>
INTERNATIONAL APPLICATION NO. <b>PCT/DE98/01172</b>	INTERNATIONAL FILING DATE <b>28 April 1998</b>	PRIORITY DATE CLAIMED <b>29 April 1997</b>
TITLE OF INVENTION: DEVICE FOR DETERMINING FLUCTUATIONS IN END EXPIRATORY GASES, METHOD FOR DETERMINING FLUCTUATIONS IN RESPIRATORY METABOLISM AND THE USE OF SAID DEVICE		
APPLICANT(S) FOR DO/EO/US <b>Ludwig WILDT; Peter LICHT; Matthias MICHEL</b>		
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:		
<p>1. <input checked="" type="checkbox"/> This is a <b>FIRST</b> submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a <b>SECOND</b> or <b>SUBSEQUENT</b> submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).</p> <p>4. <input checked="" type="checkbox"/> A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.</p> <p>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))           <ul style="list-style-type: none"> <li>a. <input type="checkbox"/> is transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>b. <input checked="" type="checkbox"/> has been transmitted by the International Bureau.</li> <li>c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US).</li> </ul> </p> <p>6. <input checked="" type="checkbox"/> A translation of the International Application into English (35 U.S.C. 371(c)(2)).</p> <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))           <ul style="list-style-type: none"> <li>a. <input type="checkbox"/> are transmitted herewith (required only if not transmitted by the International Bureau).</li> <li>b. <input type="checkbox"/> have been transmitted by the International Bureau.</li> <li>c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired.</li> <li>d. <input type="checkbox"/> have not been made and will not be made.</li> </ul> </p> <p>8. <input checked="" type="checkbox"/> A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p>		
Items 11. to 16. below concern document(s) or information included:		
<p>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A <b>FIRST</b> preliminary amendment.  <input type="checkbox"/> A <b>SECOND</b> or <b>SUBSEQUENT</b> preliminary amendment.</p> <p>14. <input type="checkbox"/> A substitute specification.</p> <p>15. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>16. <input checked="" type="checkbox"/> Other items or information (copies of the following):           <ul style="list-style-type: none"> <li>(i) Form PCT/IB/308 dated Nov. 5, 1998</li> <li>(ii) WO 98/49536</li> <li>(iii) Form PCT/ISA/210, Int. Search Report (and English-language translation thereof)</li> <li>(iv) Drawings, 2 sheets, Figs. 1 to 2</li> <li>(v) International Preliminary Examination Report, Form PCT/IPEA/409 (and English-language translation thereof)</li> <li>(vi) Article 19 claims (in German)</li> </ul> </p>		
		Express Mail Mailing Label No.: <b>EL 173 831 687 US</b> Date of Deposit: <b>October 29, 1999</b>
I hereby certify that this paper and any papers identified herein is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231		
 <b>Laraine Dobies</b>		

U.S. APPLICATION NO. <u>09/7403940</u>		INTERNATIONAL APPLICATION NO. PCT/DE98/01172	ATTORNEY'S DOCKET NUMBER 990667/RSB																								
<p>17. <input checked="" type="checkbox"/> The following fees are submitted:</p> <p><b>BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):</b></p> <table> <tr> <td>Search Report has been prepared by the EPO or JPO .....</td> <td>\$ 840.00</td> </tr> <tr> <td>International preliminary examination fee paid to USPTO (37 CFR 1.482) .....</td> <td>\$ 670.00</td> </tr> <tr> <td>No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) .....</td> <td>\$ 760.00</td> </tr> <tr> <td>Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO .....</td> <td>\$ 970.00</td> </tr> <tr> <td>International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 35(2)-(4) .....</td> <td>\$ 96.00</td> </tr> </table>				Search Report has been prepared by the EPO or JPO .....	\$ 840.00	International preliminary examination fee paid to USPTO (37 CFR 1.482) .....	\$ 670.00	No international preliminary examination fee paid to USPTO (37 CFR 1.482) but international search fee paid to USPTO (37 CFR 1.445(a)(2)) .....	\$ 760.00	Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO .....	\$ 970.00	International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 35(2)-(4) .....	\$ 96.00														
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<p>Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)).</p>																											
<table border="1"> <thead> <tr> <th>CLAIMS</th> <th>NUMBER FILED</th> <th>NUMBER EXTRA</th> <th>RATE</th> </tr> </thead> <tbody> <tr> <td>Total claims</td> <td>11 - 20 =</td> <td>0</td> <td>* 18.00</td> </tr> <tr> <td>Independent claims</td> <td>2 - 3 =</td> <td>0</td> <td>* 78.00</td> </tr> <tr> <td>MULTIPLE DEPENDENT CLAIM(S) (if applicable)</td> <td></td> <td></td> <td>+ 260.00</td> </tr> <tr> <td colspan="3"><b>TOTAL OF ABOVE CALCULATIONS</b></td> <td><u>\$ 840.00</u></td> </tr> </tbody> </table>				CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	Total claims	11 - 20 =	0	* 18.00	Independent claims	2 - 3 =	0	* 78.00	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ 260.00	<b>TOTAL OF ABOVE CALCULATIONS</b>			<u>\$ 840.00</u>				
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<p>Reduction of 1/2 for filing by small entity, if applicable. Verified Small Entity Statement must also be filed (Note 37 CFR 1.9, 1.27, 1.28).</p>																											
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<p>a. <input checked="" type="checkbox"/> A check in the amount of <u>\$ 840.00</u> to cover the above fees is enclosed.</p>																											
<p>b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of <u>\$</u> _____ to cover the above fees. A duplicate copy of this sheet is enclosed.</p>																											
<p>c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>06-1378</u>. A duplicate copy of this sheet is enclosed.</p>																											
<p><b>NOTE:</b> Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.</p>																											
<p>SEND ALL CORRESPONDENCE TO:</p> <p>FRISHAUF, HOLTZ, GOODMAN, LANGER &amp; CHICK, P.C. 767 Third Avenue - 25th Floor New York, NY 10017-2023 Tel. No. (212) 319-4900 Fax No. (212) 319-5101</p>																											
<p>SIGNATURE <u>Richard S. Barth</u></p>																											
<p>NAME <u>28,180</u></p>																											
<p>REGISTRATION NUMBER</p>																											
<p>Date: <u>October 29, 1999</u></p>																											

Nov. 17. 1999 11:00AM FRISHAUF & PARTNERS

No. 2820 P. 5/5  
From: BARTH

Applicant : Ludwig WILDT et al.

Attorney's Docket No: 990667/RSB

Serial No.: 09/403,940

Filed : Deposited on October 29, 1999

Title: DEVICE FOR DETERMINING FLUCTUATIONS IN END EXPIRATORY GASES, METHOD FOR DETERMINING FLUCTUATIONS IN RESPIRATORY METABOLISM AND THE USE OF SAID DEVICE

STATEMENT CLAIMING SMALL ENTITY STATUS (37 CFR 1.9(f) and 1.27(b) - INDEPENDENT INVENTOR

As a below named inventor, I hereby declare that I qualify as an independent inventor as defined in 37 CFR 1.9(c) for purposes of paying reduced fees under 35 USC 41(a) and 41(b) of Title 35, United States Code, to the Patent and Trademark Office with regard to the invention described in

1. [ ] the specification filed herewith; or
- [X] application above identified; or
- [ ] patent above identified.

2. [X] Other than among the coinventors set forth hereinbelow, we have not assigned, granted, conveyed or licensed and are under no obligation under contract or law to assign, convey or license, any rights in the invention.

3. [ ] Each person, concern or organization to which I have assigned, granted, conveyed, or licensed or am under an obligation under contract or law to assign, grant, convey or license any rights in the invention and who is entitled to pay reduced fees under 35 USC 41(a) and 41(b), is listed below:

\*NOTE: Separate qualified statements are required from each named person, concern or organization having rights to the invention availing to their status as small entities. (37 CFR 1.27)

FULL NAME WILDT, Ludwig

ADDRESS Haundorfer Str.2b, D-91074 Herzogenaurach, DE  
[X] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

FULL NAME MICHEL, Matthias

ADDRESS K.-H.-Flach-Str.32, D-61440 Oberursel, DE  
[X] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

FULL NAME LICHT, Peter

ADDRESS Dompfaffstr.5, D-91088 Bubenreuth, DE  
[X] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NONPROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b) )

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

Ludwig WILDT  
NAME OF INVENTOR

Peter LICHT  
NAME OF INVENTOR

Matthias MICHEL  
NAME OF INVENTOR

Signature of Inventor

Signature of Inventor

Signature of Inventor

23.12.99  
Date

23.12.99  
Date

20.12.99  
Date

09/40394

514 Rec'd PCT/PTO 29 OCT 1999

Attorney Docket No. 990667/RSB

**IN THE UNITED STATES PATENT  
AND TRADEMARK OFFICE**

Applicant : Ludwig WILDT et al.

Serial No. : To be assigned (U.S.  
National Phase of  
PCT/DE98/01172, filed  
April 28, 1998)

Filed : Concurrently Herewith

For : DEVICE FOR DETERMINING  
FLUCTUATIONS IN END  
EXPIRATORY GASES, METHOD  
FOR DETERMINING  
FLUCTUATIONS IN RESPIRATORY  
METABOLISM AND THE USE ...

Art Unit :

Examiner :

**PRELIMINARY AMENDMENT**

Assistant Commissioner for Patents  
Washington, D.C. 20231

**ATTENTION: BOX PCT**

S I R :

Please amend the application as follows:

**IN THE SPECIFICATION:**

Page 1, before line 1 (after the title), insert the

following:

--BACKGROUND OF THE INVENTION

Field of the Invention--;

between lines 4 and 5, insert the following:

--Background Information--;

line 16, replace "e.g." with --, e.g.,--.

Express Mail Mailing Label

No.: EL 173 831 687 US

Date of Deposit: October 29, 1999

I hereby certify that this paper is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231

*Laraine Dobies*

Laraine Dobies

In the event that this Paper is late filed, and the necessary petition for extension of time is not filed concurrently herewith, please consider this as a Petition for the requisite extension of time, and to the extent not tendered by check attached hereto, authorization to charge the extension fee, or any other fee required in connection with this Paper to Account No. 06-1378.

**Page 2**, line 4, replace ".It" with --, it--;  
line 7, replace "i.e." with --, i.e.,--;  
line 8, after "diseases" insert --of the--;  
line 9, replace "e.g." with --, e.g.,--;  
line 13, replace "i.e." with --, i.e.,--;  
line 17, replace CO<sub>2</sub>/O<sub>2</sub>" with --CO<sub>2</sub>/O<sub>2</sub>--;  
line 19, replace "e.g." with --, e.g.,--.

**Page 3**, lines 2, 7, 9 and 10, replace "pCO<sub>2</sub>" with "pCO<sub>2</sub>";  
line 4, delete "rhythmical"; same line, replace  
"body temperature" with --cycle--;  
line 10, delete "such"; same line, before "few"  
insert --a--;  
line 15, replace "e.g." with --, e.g.,--.  
line 20, delete "such".

**Page 4**, line 3 after "i.e." insert --,--; same line, replace  
"pCO<sub>2</sub>" with --pCO<sub>2</sub>--;  
line 4, after "e.g." insert --,--;  
between lines 8 and 9, insert the following:  
--SUMMARY OF THE INVENTION--;  
line 11, after "device", delete ",,";  
line 16, after "i.e." insert --,--.

**Page 5**, lines 1 and 11, after "e.g." insert --,--;  
line 9, replace "only necessary" with  
--necessary only--;  
line 12, delete "Preferred embodiments can be  
taken from the dependent claims.";  
line 15, replace "CO<sub>2</sub>" with --CO<sub>2</sub>--;  
line 16, replace "gas/es" with --gas/gasses--.

**Page 6**, line 7, after "fluctuations", insert --,--;  
line 10, before "a comparison", insert --to provide--;  
line 11, replace "e.g." with --, e.g.,--;  
lines 16 and 17, replace "pCO<sub>2</sub>" with --pCO<sub>2</sub>--.

**Page 7**, line 16, replace "e.g." with --, e.g.,--;  
line 19, replace "with measurement of" with  
--measure--.

**Page 8**, lines 2, 7, 8, 10, 13, 15 and 22, replace "pCO<sub>2</sub>"  
with --pCO<sub>2</sub>--;  
line 12, replace "i.e." with --, i.e.,--;  
line 14, replace "CO<sub>2</sub>" with --CO<sub>2</sub>--;  
line 22, replace "pO<sub>2</sub>" with --pO<sub>2</sub>--.

**Page 9**, between lines 6 and 7, insert the following:

--BRIEF DESCRIPTION OF THE DRAWINGS--;

line 7, delete "with";

line 8, replace "drawing" with --drawings--;

line 11, replace "pCO2" with --pCO<sub>2</sub>-- ;

between lines 11 and 12, insert the following:

--DETAILED DESCRIPTION OF THE INVENTION--;

line 12, before "cycle" insert --a--; same line,

after "computer" insert --,--;

lines 18 and 19, replace "CO2" with --CO<sub>2</sub>--;

last line, replace "pCO2" with --pCO<sub>2</sub>--.

**Page 10**, line 2, replace "pCO2" with --pCO<sub>2</sub>--;

line 3, replace "Sensors" with --sensors--; same

line, after "temperature" insert --,--;

lines 7 and 9, after "i.e." insert --,--;

line 8, replace "CO2" with --CO<sub>2</sub>--.

**IN THE CLAIMS:**

Please cancel original claims 1 to 17, without prejudice.

Please add the following claims:

18. A method for monitoring in an animal or a human,  
hormonal fluctuations, ovulation prediction, breathing function,

the extent of physical fitness, the progress of pharmacological therapies or the progress of oxygen-therapy, the method comprising:

- (a) obtaining a volume of an end expiratory gas mixture from an animal or a human,
- (b) determining the amount of one or more gases contained within said volume,
- (c) recording of the value thus obtained in step (b), optionally together with time data and individual data,
- (d) comparing values from step (c) with a table of values, and
- (e) generating a signal according to the comparing of values in step (d), said signal being stored or optionally being processed and/or edited.

**19.** The method according to claim 18, wherein the gas determined in step (b) is at least one gas selected from the group consisting of CO<sub>2</sub> and O<sub>2</sub>.

**20.** The method according to claim 18, wherein the amount of the at least one gas in the end expiratory gas mixture is optically determined.

**21.** The method according to claim 20, wherein the method is for predicting ovulation and the at least one gas is CO<sub>2</sub>.

**22.** The method according to claim 18, wherein stored measured data are compared with already stored data by a program, wherein detection of a deviation from a predetermined value provides the signal.

**23.** A device for the determination of the partial pressure of at least one gas in an end expiratory mixture of gases from an animal or a human or for predicting ovulation, the device comprising:

- (a) a receiving unit for receiving a gas volume of end expiratory gas from an animal or a human,
- (b) at least one measuring device for the determination of the at least one gas in the end expiratory gas volume received in the receiving unit, and for the generation of measurement signals, and
- (c) a unit for display and/or storage and evaluation for recording and processing of signals received from the at least one measuring device, wherein the measured values therefrom are stored together with individual data of the animal or human being monitored.

**24.** The device according to claim 23, which further comprises an optical measuring unit to determine the IR absorption of CO<sub>2</sub>, wherein the measuring unit provides a signal that is stored together with time data or the identity of the animal or human, in a memory.

25. The device according to claim 23, wherein the optical measuring unit is an IR measuring cell.

26. The device according to claim 23, which further comprises an oxygen sensor.

27. The device according to claim 23, which further comprises a device to absorb water from the end expiratory gas.

28. The device according to claim 23, which further comprises a portable energy source.

**IN THE ABSTRACT:**

Please replace the ABSTRACT with the ABSTRACT OF THE DISCLOSURE attached hereto.

R E M A R K S

The specification was editorially revised.

New claim 18 includes features from original claims 15 and 17.

New claim 19 includes features from original claim 14.

New claim 20 includes features from original claim 15.

New claim 21 includes features of claims 18 and 19.

New claim 22 includes features of original claim 8.

New claim 23 includes features of original claims 1 and 4.

New claim 24 includes features of original claims 2, 3 and 5.

New claim 25 includes the feature of original claim 3.

New claim 26 includes features of original claim 5.

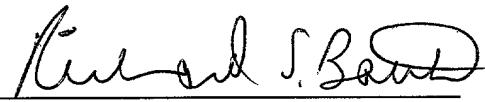
New claim 27 includes the feature of original claim 6.

New claim 28 includes the features of original claim 12.

If the Examiner has any comments, questions, objections or recommendations, the Examiner is invited to telephone the undersigned at the telephone number given below for prompt action.

FRISHAUF, HOLTZ, GOODMAN,  
LANGER & CHICK, P.C.  
767 Third Avenue, 25th Floor  
New York, NY 10017-2023  
Tel. No. (212) 319-4900  
Fax No. (212) 319-5101  
RSB/jh/ld

Respectfully submitted,

  
RICHARD S. BARTH  
REG. NO. 28,180

ABSTRACT OF THE DISCLOSURE

A method for monitoring in an animal or a human, hormonal fluctuations, ovulation prediction, breathing function, the extent of physical fitness during exercise, the progress of pharmacological therapies or the progress of oxygen-therapy, the method comprising: (a) obtaining a volume of an expiratory gas mixture from an animal or a human, (b) determining the amount of one or more gases contained within said volume, (c) recording of the value thus obtained in step (b), optionally together with time data and individual data, (d) comparing values from step (c) with a table of values, and (e) generating a signal according to the comparing of values in step (d), the signal being stored or optionally being processed and/or edited.

Device for determining end expiratory gases, method for determination of fluctuationsin respiratory metabolism and the use of the device

The invention relates to a device for the determination of the partial pressure of at least one gas in a end expiratory gas mixture; a method for the monitoring of fluctuations in respiratory metabolism in the animal or human body and to the use thereof.

The partial pressure of different gases in end expiratory gas mixtures is dependent upon various functions of the body - inter alia from hormonal fluctuations, disorders disturbing the respiratory metabolism such as asthma, mucoviscidosis etc. as well as upon the energy balance of the body (respiratory quotient). In various metabolic disorders or in recreatory drug abuse certain metabolic products can be detected in the end expiratory gas (diabetes, alcohol-abuse). Further the aforesaid changes during severe physical stress and therefore is an indicator for the physical ability of the body (fitness).

Especially the end expiratory gas mixture - that is the last gas volume exhaled, is an exact picture of the alveolar partial gas pressure that is again dependent on various body functions.

Until now complicated devices for measuring the actual partial gas pressure e.g. in anesthesiology have been known to measure the actual end expiratory gas pressure there. The values measured were only momentarily of interest - storage or evaluation of the stored values during a time interval was not possible. Further the known instruments were complicated and not suited for private use but for the needs of operation room conditions.

It has been found surprisingly that by measuring the end expiratory gases - especially the end expiratory gases and evaluation thereof for body functions and metabolism can be monitored also outside of an operation room/intensive care station.

The device can be used preferably for monitoring the respiratory function. It is understood thereunder especially such disorders/conditions of the body that alter the gas content of blood. Such like asthma, chronic lung emphysema, oxygen therapy, fitness status of an athlete i.e. for detecting the limits of performance, sleep apnoea including chronical; snoring, and inflammatory diseases respiratory tract.

Moreover in therapies with drugs that influence the respiratory center e.g. barbiturates, progesterone and derivatives thereof, narcotics and analgetics the actions thereof can be monitored. As well a monitoring of persons in closed rooms, such as astronauts, plungers, submarine-drivers, workers in caissons is possible.

Thereby inter alia an impairment of the function of gas exchange, i.e. the development of a chronic or acute respiratory failure, monitoring and optionally adjustment of therapy - oxygen therapy, hormonal treatment or other drug treatments can be determined.

With the ratio of CO<sub>2</sub>/O<sub>2</sub> in the end expiratory volume (lungemphysem quotient) also the status of metabolism, like progress of a dietetic measure or the fitness (efficiency degree of the body) e.g. in competitive athletes or also in physical rehabilitation measures can be monitored.

A particular interesting application is the monitoring of the lung emphysema in blood by determining pCO<sub>2</sub>. Since Döring: Pflügers Archiv 250 (1948), pp. 37 - 46 "About rhythmical fluctuations of breathing and body temperature in the menstrual cycle" and Döring, G. K. "About rhythmical fluctuations of respiration and body temperature" Arch Gynäkol. 182 (1953), pp 746 - 758 and Döring, GK, H.J.H. Loeschke, B. Ochwaldt: "Further tests about the effects of the sexual hormones on respiration" Pflügers Archiv 252 (1950), pp 216 - 230 it is known that the pCO<sub>2</sub> in women fluctuates during the menstrual cycle influenced by progesterone. It is especially significant, that in women significantly 3 - 4 days before ovulation a decline of pCO<sub>2</sub> appears. The end expiratory pCO<sub>2</sub> such declines few days just before the ovulation - influenced by the rising progesterone level in blood and stays high during the luteal phase of the menstrual cycle and in pregnancy in consequence to an increased alveolar ventilation.

It has not been tried until now to use this medical phenomenon for the production of measuring devices.

Devices for ovulation detection, e.g. so called "cycle computers" that evaluate measurements of the basal body temperature or determinations of the luteinizing hormone (LH) by biochemical color reactions have always been inaccurate or gave information only very near or after the ovulation, which is useless for contraception or for the lung emphysema.

Further basal body temperature measurement is very easily such strongly influenced by "external circumstances" - like physical activity, disorders with fever, drugs, short sleeping period, time shifts due to air plane travel - that the measured value often is useless and thus can be used for the prediction of ovulation only with very high faults. So the known devices had the deficiency of being too inaccurate and further evaluated

body function data that can be altered strongly by the life circumstances of the patient, so that the measurement was not reliable. Further it may be interesting to monitor the fluctuations in progesterone - i.e. the pCO<sub>2</sub> controlled thereby during a risk pregnancy (e.g. asthma patient), to be able to manifest a decline of progesterone which endangers the pregnancy and optionally to be able to take counter-measures.

Nevertheless the measurement of other gases in the end expiratory gas can be interesting - especially as the values are readily obtained and are independent of time-consuming detection-reactions in laboratories.

It is an object of the invention to provide a device for determination/evaluation of partial pressures of gases in an end expiratory gas volume.

According to the invention the object is met by a device, that measures end expiratory gases, comprising: a receiving unit for the receiving of end expiratory gas, a measurement unit to determine the at least one gas in the thus received volume of end expiratory gas and to generate measurement signals; and a processor unit for storing and further processing of the signals measured in a predetermined time interval.

First this processor unit selects suitable measurement signals - i.e. such that are at the end of the exhalation process, as the values there are more stable and optionally an end expiratory value and effects the editing of this selected measured value into memory - optionally together with individual data about the measurement date, the measurement time, the individual herself and optionally also a further processing of the aforesaid signals by comparison with stored values. Optionally the stored values may be edited on a printer, readable and storable on conventional transportable data carriers known per se or by remote inquiry. Also a processing of individually selected

measurement values may be provided in the device - e.g. comparison with a stored measurement value table and display when deviations from the stored values greater than a predetermined threshold occur. It is also possible to monitor the variation of the values with time and to edit only the values resulting therefrom.

Preferably this unit is portable, of small dimensions and optionally battery-powered, so that it may be used on different places of the stay of the monitored individual.

Of course the device may be provided such that it measures several partial gas pressures simultaneously or sequentially - if a measurement of several gas pressures is desired. To this effect it is only necessary to measure different absorption bands of the gases at different places and to evaluate or to use a suitable measurement method for each gas.- e.g. commercial oxygen sensors for oxygen.

Preferred embodiments can be taken from the dependent claims.

It is advantageous if the physical measuring unit is an optical measuring unit, as optical determinations are fast and are easily converted into electrical signals.

For the measurement of polar gases, like CO<sub>2</sub>, it is especially preferred that the measuring cell is an IR-measuring cell, measuring an absorption band of the gas/es to be determined in a predetermined absorption wavelength area that is not absorbed by other gases, and to determine the concentration of the gas in the gas volume in a manner known per se. The invention is not delimited to IR-spectroscopic measurements - Raman spectroscopy, conductivity measurements, etc. and also usual gas sensors may be used to determine one gas in the gas mixture.

For the evaluation of a history it may be advantageous, that the values measured in a predetermined time interval are stored in a memory, that optionally may be read by an editing unit.

Typically the device has a printer as an editing unit, a readable display and/or a memory chip, that is computer-readable, so that either the value may be read visually concurrently or that the history of the values as such can be evaluated or read later.

In the special case of cycle monitoring or determination of other hormonal fluctuations now histories of the fluctuations of the measured values can be stored together with measurement data (time, atmospheric pressure etc.) and edited - whereby complicated stationary tests can be avoided. Thereby is possible only now a comparison of different tests over a longer period of time - like cycle data. Further e.g. constant monitoring of the progress of a risk gestation with time is possible, without the patient having permanently to undergo complicated tests. The inventive device is especially suited for the monitoring of the pretreatment for in vitro fertilization and other procedures of assisted reproduction.

To meet this object the device may measure pCO<sub>2</sub> in the end expiratory gas only. It is preferred to determine pCO<sub>2</sub> by IR-absorption of a predetermined end expiratory gas volume in a measuring cell and to compare these values preferably either with individual basis data of the individual or to monitor only its relative fluctuation over a time interval.

As the amount of gas and thus the number of absorbing molecules in a gas volume is temperature-dependent, it is useful to thermostatate the measurement cell. Otherwise

the measured value may be compensated by computation by means of temperature value measured by a sensor in the measurement cell, whereby complicated thermostatization may be avoided - this may be especially useful in applications with high temperature fluctuations.

Preferably further a measurement unit for atmospheric pressure at the measurement time is provided and by means of the measurement the result of the measurement may be corrected for atmospheric pressure. Thereby obtaining measurement values falsified by pressure variations can be avoided. The device itself can be designed in a manner known per se as two-beam photometer.

An especially preferred use of the inventive device is the prediction of the ovulation. To such a purpose a memory for storing cycle data - optionally together with other measurement data, like temperature, is provided, that gives readings accordingly. The measured data are each compared with preceding measured data within a predetermined time interval and it is determined, whether significant deviation occurs. Thereby predication of the ovulation about three days in advance is possible - a method that is much more precise for contraception or conception than e.g. measurement of temperature, being strongly dependent on physical activity, time of the day etc. of the individual monitored.

Compared with known cycle computers that normally with measurement of the basal temperature, that is easily disturbed and thus often is imprecise, the inventive device has the advantage of a fast and precise determination independent from events like short sleeping period, physical activity etc.

A further preferred use of the device is the monitoring of pregnancy. The lowering of pCO<sub>2</sub> is typical for a normal gestation and a rise thereof is a sign of a severe disorder.

To obtain the end expiratory gas, that alone is an exact picture of the alveolar status, a device may be installed, that forces the patient to exhale completely - then only those measured values are evaluated, that have been taken in the last time interval of expiration. Therefore especially units forcing the individual to exhale against an obstacle, like when inflating a balloon or the like, where the highest measured pCO<sub>2</sub> is this significant end expiratory pCO<sub>2</sub> - this may be determined in a manner known per se by a processing unit programmed accordingly, that records the measured values and evaluates the aforesaid, so that only the highest pCO<sub>2</sub> per breathing event is stored/displayed.

The process for the prediction of the ovulation i.e. of progesterone on basis of the end expiratory pCO<sub>2</sub> comprises: obtaining of a volume of end expiratory gas; determination of the IR-Absorption of the CO<sub>2</sub>-band in the gas volume of end expiratory gas and thus determination of the pCO<sub>2</sub> therein, correction of the result for the atmospheric pressure and temperature and editing of the measured value into an editing unit, like a memory, a printer, a display.

It may be useful to remove water vapor from the exhaled gas by absorption or condensation before the measurement cell, to obviate falsifications of the measurement result by condensation on the windows of the measurement cell.

For the use in other fields, e.g. for the monitoring of respiratory function or of fitness it is necessary to measure pCO<sub>2</sub> and pO<sub>2</sub> and to form the ratio thereof. This ratio may either be stored as such or be edited or optionally compared with predetermined ratios

of the same individual or with basis data already in the device and when crossing a predetermined threshold value a signal is generated.

This signal enables the individual or his trainer (if the device is used for monitoring physical training) to alter his performance so that the body is working again in its normal range. Nevertheless, the signal may be used for controlling therapeutic measures.

In the following the invention shall be illustrated in more detail with under consideration of the annexed drawing, that shows schematically an embodiment of the invention for cycle monitoring, whereas it is not meant that it be delimited thereto, shows:

Fig. 1: an embodiment of an inventive device in schematic representation; and

Fig. 2: a graph depicting pCO<sub>2</sub> dependent from cycle history.

Referring now to Fig. 1 in a preferred embodiment of the invention as cycle computer an inventive device comprises an IR-radiation source, the radiation thereof is directed through a gas measurement cell. In this measurement cell end expiratory gas is blown, that optionally may be dried in a manner known per se, to obviate condensation on the windows of measurement. The radiation emitted from the measurement cell is filtered by means of an optical filter onto the absorption area of the gas to be measured - in this case CO<sub>2</sub> - and the radiation in the predetermined area of the IR-absorption band of CO<sub>2</sub> is directed onto an IR-sensor. Preferably the signal of the sensor is amplified in a manner known per se and then is either stored with further cycle data of the individual/further processed or simply edited on a display. It is useful that the device is enabled by a processor contained therein to store a pCO<sub>2</sub> value of an exhaled volume

only, if the aforesaid does not change much any more, to obtain an end expiratory pCO<sub>2</sub> value. In the embodiment with IR-Sensors by measurement of the temperature the influence of temperature is compensated for by computation in a manner known per se. On the other hand it is possible to climatize the measurement cell itself. The measurement of the gas is also compensated for atmospheric pressure.

Preferably the device is small and portable and may be easily transported by the user.

From Fig. 2 the physiological basis of the cycle computer may be seen, i.e. that the CO<sub>2</sub> partial pressure declines significantly already about 3 - 4 days before the normally obtained values, i.e. the peak of the luteinizing hormone (LH) and of estradiol (E2) and of basal temperature and such enables a very simplified and ameliorated and especially earlier detection of the expected ovulation compared with known devices ("cycle computer").

Further embodiments and developments are obvious to the expert in the field within the scope of the claims and the scope of protection shall not be delimited to the examples, that have been referred to for illustration purposes only.

**(New) Claims (ARTICLE 19)**

**1. Use of a device for determining the partial pressure of at least one gas in a mixture of end expiratory gases comprising:**

- a receiving unit for receiving a volume of end expiratory gases**
- at least one measuring device for the determination of at least one gas in the received end expiratory gas volume and to generate signals; and**
- a unit for storage and evaluation for receiving and processing of the signals of the at least one measuring device for the determination of hormonal fluctuations, of the physical fitness during exercise as well as of pharmacological therapies and for the monitoring of oxygen therapy.**

**2. Use according to claim 1, characterized therein, that the determination of hormonal fluctuations is performed in human individuals.**

**3. Use according to claim 2, characterized therein, that the determination of hormonal fluctuations is monitoring of the menstrual cycle, especially of the time of ovulation.**

**4. Method for monitoring hormonal fluctuations in animal and human body, the physical fitness during exercise as well as of pharmacological therapies and for monitoring of oxygen-therapy characterized by the steps:**

- obtaining a volume of an end expiatory gas mixture**

- determination of the amount of one or more gas/es contained within this volume

- recording of the value thus obtained, optionally together with data of the time and individual data

- comparison of the aforesaid value/s with a table of values and

- generation of a signal according to the comparison step, that may be stored, optionally further processed and/or edited.

5. Method according to claim 4, characterized therein, that the gas determined is CO<sub>2</sub> and/or O<sub>2</sub>.

6. Method according to claim 4 or 5, characterized therein, that the amount of at least one gas in the end expiratory gas mixture is determined optically.

7. Device for the determination of the partial pressure of at least one gas in an end expiratory mixture of gases for the use according to one of the claims 1 - 4, comprising:

- a receiving unit for the receiving of a volume of end exspiratory gas

- at least one measuring device for the determination of at least one gas in the received end expiratory gas volume and to generation of measurement signals and

- a unit for storage and evaluation for recording and processing of the signals of at least one measuring device, wherein the measured values are stored together with datum, individual data of the individual monitored.

8. Device according to claim 7, characterized therein, that it comprises an optical measuring unit, especially an IR-measuring cell to determine the IR absorption of CO<sub>2</sub>, wherein the signal of the IR-measuring cell is stored together with time data, like datum, time or the name of the patient in a memory.

9. Device according to claim 8, characterized therein, that the individualized stored measured data are comparable with already stored data by means of a program, wherein the detection of a deviation from a predetermined value will lead to a signal.

10. Device according to any one of the preceding claims 7 to 9, characterized therein, that it comprises an oxygen sensor.

11. Device according to one of the claims 7 - 10, characterized therein, that it comprises a device to absorb water from the end expiratory gas.

12. Device according to one of the claims 7 - 11, characterized therein that it comprises an own energy source and that it is portable.

## ABSTRACT

The invention relates to a device for determining the partial pressure of at least one gas in an end expiratory gas mixture, comprising a receiving unit for a volume of end expiratory gas, at least one measuring device to determine the volume of an end expiratory gas received therein and to output measuring signals, in addition to display and/or storage and evaluation unit to receive and process the signals of the at least one measuring device. The invention also relates to a method for monitoring fluctuations in respiratory metabolism of the human or animal body and to the use thereof in determining respiratory function.

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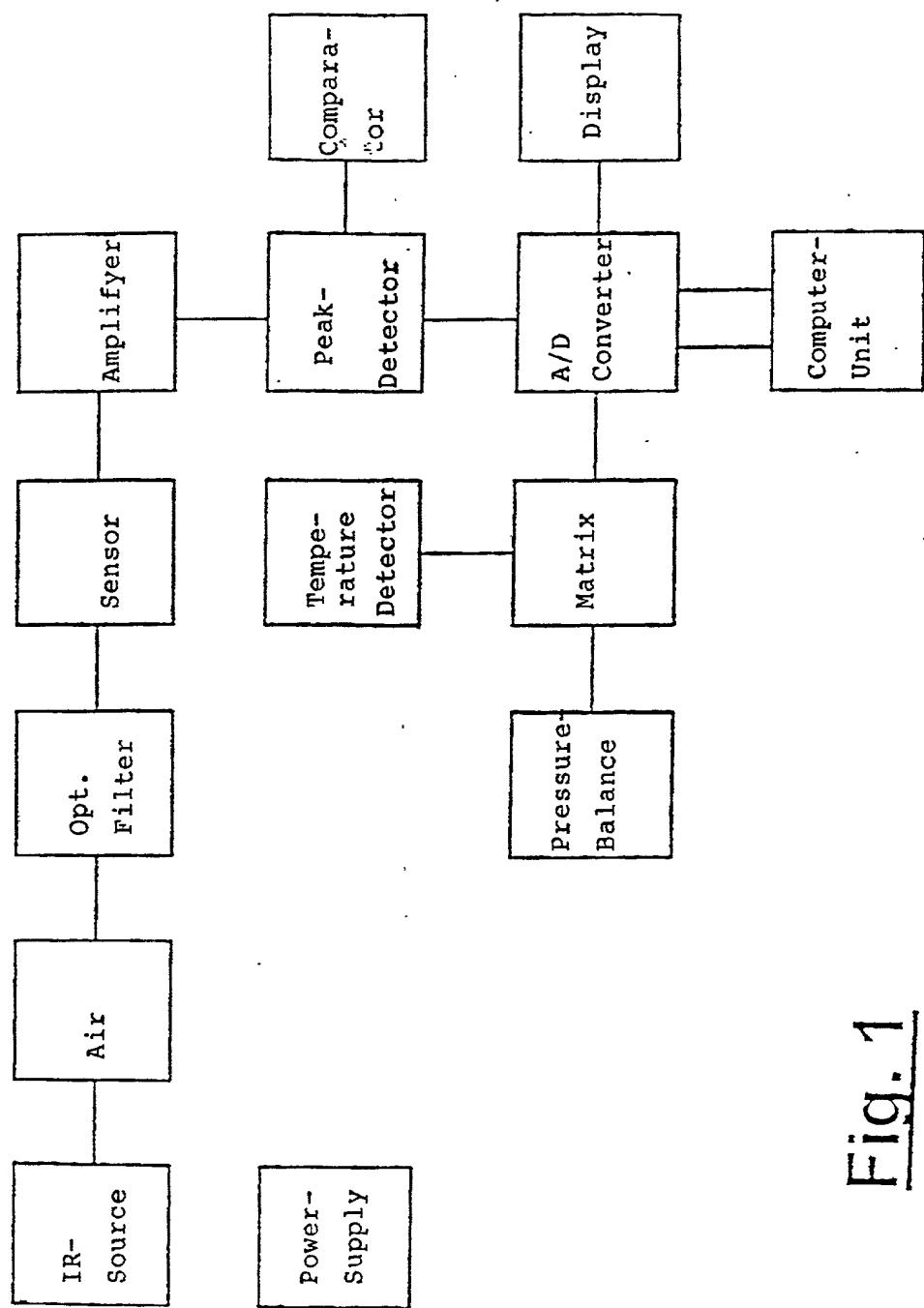


Fig. 1

09/40340

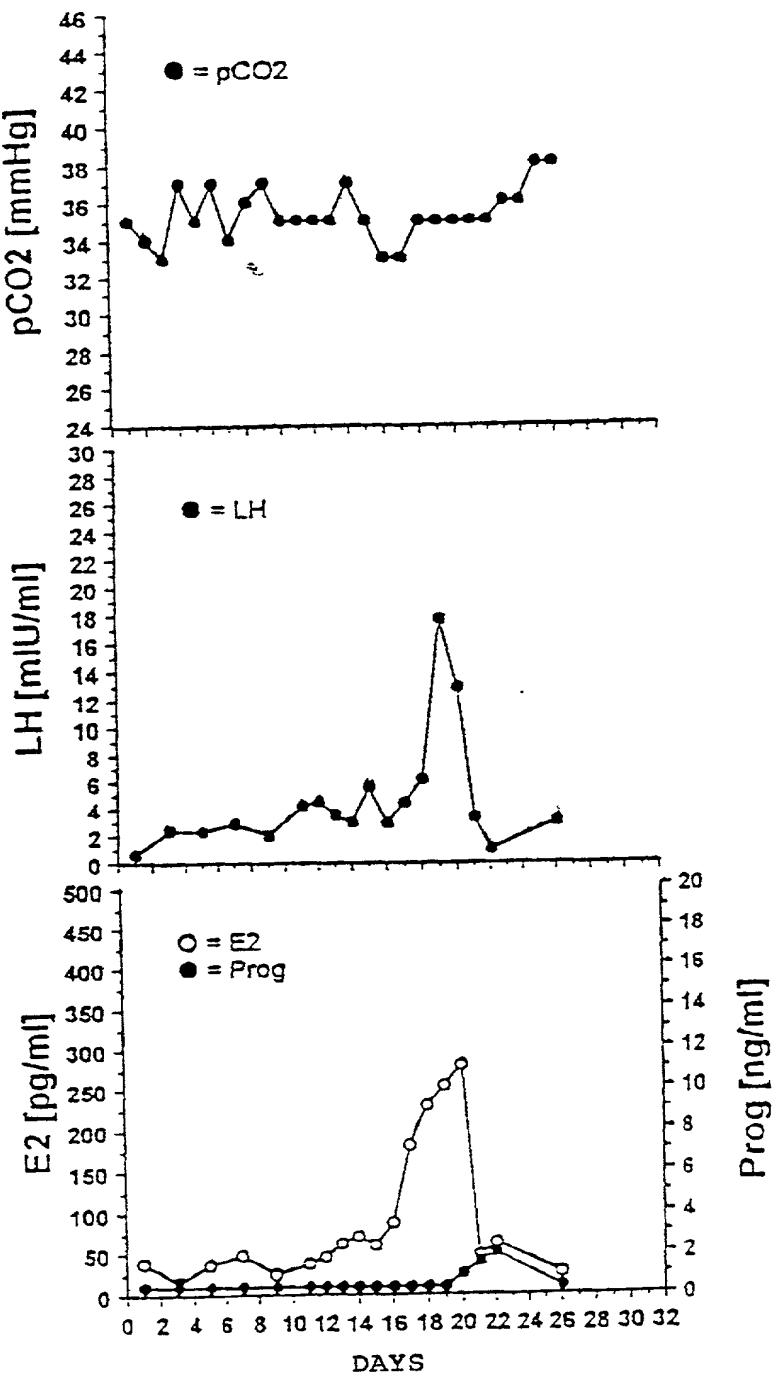


Fig. 2

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No. 2820 P. 4/5

U.S. Atto From: BARTH 0667/RSB

**APPLICATION FOR UNITED STATES LETTERS PATENT**  
**POST-FILED PCT Declaration and Power of Attorney (35 U.S.C. 371(c)(4))**  
**PCT Application - United States Designated Office**

As a below named inventor, I declare that:

My residence, post office address and citizenship are as stated below next to my name; I believe that I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

**DEVICE FOR DETERMINING FLUCTUATIONS IN END EXPIRATORY GASES, METHOD FOR DETERMINING FLUCTUATIONS IN RESPIRATORY METABOLISM AND THE USE OF SAID DEVICE**  
described and claimed in serial number 09/403,940 deposited October 29, 1999, which is the national phase application of international application number PCT/DE98/01172, filed April 28, 1998.

I have reviewed and understand the contents of said specification, including claims.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 CFR §1.56.

I claim priority benefits under 35 USC §119 of: (i) any foreign application(s) for patent or inventor's certificate listed below; or (ii) any United States provisional application(s) listed below; and have also identified below any foreign application(s) for patent or inventor's certificate, or PCT international application having a filing date before that of the application(s) on which priority is claimed.

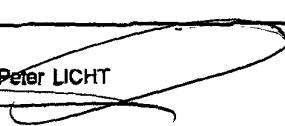
COUNTRY	APPLICATION NUMBER	DATE (day, month, year)	PRIORITY CLAIMED
Germany	297 07 771.6	29, April, 1997	yes <input checked="" type="checkbox"/> no _____

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I appoint the following attorneys to prosecute this application and to transact all business in the U.S. Patent & Trademark Office connected therewith: Leonard Holtz, Reg. No. 22,974; Herbert Goodman, Reg. No. 17,081; Thomas Langer, Reg. No. 27,264; Marshall J. Chick, Reg. No. 26,853; Richard S. Barth, Reg. No. 28,180; Douglas Holtz, Reg. No. 33,902; and Robert P. Michal, Reg. No. 35,614.

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